

ease progression. Real-world data on actual health care resource consumption and patient clinical characteristics are used. Time horizon of the models should be long enough to capture meaningful differences in outcomes. The differential clinical attributes of the products are identified and direct links are established with the corresponding economic values. The resulting impact on disease progression and consequences for consumption of health care resources are simulated. The primary output is the cost-avoidance against the chosen comparator, with corresponding breakdown by each clinical attribute. **RESULTS:** CCEV directly translates the differences in clinical outcomes to the differences in economic values. This methodology has been effectively applied in the decision process at different stages of drug development, such as, to prioritize pipeline assets by comparing the potential economic value of assets under development and quantifying the value of each differentiated output. These insights are used to guide and design the following data generation strategies. **CONCLUSIONS:** CCEV methodology directly translates clinical outcomes to economic values and is a practical PE tool for decision makers. It can be employed across the entire product life-cycle, starting from the early stages of drug development.

PRM45

ARE MINIMAL CLINICALLY IMPORTANT DIFFERENCE MEASURES (MCIDS) RELEVANT FOR SURVIVAL OUTCOMES? INTRODUCING THE MCID-CAC

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Minimal Clinically Important Difference margins (MCIDs) are being applied by reimbursement agencies to assess the non-inferiority of new medications against comparator medications in the Asia Pacific Region. If a new medication is deemed non-inferior to an all ready reimbursed medication either via direct or indirect comparison methods the newer product is generally reimbursed at the same price as the comparator medication (ie. through cost-minimisation). The concept of an MCID margin for survival outcomes, however, is problematic and controversial. A superficial consideration of MCIDs for survival outcomes may lead to the conclusion that the MCID for survival is inappropriate and no difference in survival is acceptable. As such, the MCID for survival should be zero. In this case such an analysis would become a superiority analysis. If this approach to the assessment of such products were to prevail, new products with a high likelihood of affording patients a survival benefit compared to their comparator products may be rejected even on a cost-minimisation basis. Instead, where the point estimate of treatment effect favours the new treatment serious consideration should be given to reimbursing the new product at the same or higher price. Using indirect comparison methods and real world hazard ratio data this research introduces the concept of MCID-cumulative acceptability curves (MCID-CAC) as an aid to making pragmatic reimbursement decisions for new products that may extend patients lives.

DISEASE-SPECIFIC STUDIES

CANCER-Clinical Outcomes Studies

PCN1

BISPHOSPHONATES AND RISK OF OSTEONECROSIS OF JAW IN CANCER PATIENTS: A META-ANALYSIS

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OBJECTIVES: This meta-analysis aims to assess the potential risk of osteonecrosis of jaw and bisphosphonate use in cancer patients. **METHODS:** The published literature was systematically searched and reviewed using MEDLINE (1950 through July 2011), EMBASE (1980 through July 2011), and the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2011 issue 1). Studies that included specific risk estimates were pooled using a random-effects model. The bias and quality of these studies were assessed with RevMan statistical software (version 5.0) and the GRADE method of the Cochrane Collaboration. **RESULTS:** A total of 32 publications met inclusion criteria, but only 9 studies that included 51580 subjects for analysis. No randomized controlled clinical trials, meta-analysis or quality of life articles were found that contained data for risks or prevalence of osteonecrosis. The results of a meta-analysis that pooled data from 10 cohort studies indicated that the overall multivariable odds ratio and hazard ratio were 1.11 (95% CI: 0.15, 8.47) and 0.35, 23835, respectively (95% CI 0.51 to 1.00; $p = 1.00$), respectively. The risk of osteonecrosis associated with biophosphonate was statistically significant. The results of the quality assessment of these studies indicated low scores using the GRADE method. **CONCLUSIONS:** The uses of bisphosphonates is likely to be associated with the increased risk of osteonecrosis of jaw in cancer patients.

PCN2

THE RELATIONSHIP OF FOLLOWING LIPID-LOWERING DRUGS USED WITH ADJUVANT HORMONAL THERAPY IN BREAST CANCER WOMEN

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OBJECTIVES: Extended adjuvant hormonal therapy with aromatase inhibitors (AIs) or tamoxifen can both effectively reduce the recurrence of breast cancer, but the potential of change lipid profile with AIs compared to tamoxifen was observed in some clinical studies. The aim of this study was to evaluate whether the hormone adjuvant therapy will increase the prescribing rate of lipid-lowering drugs (LLDs) in breast cancer women. **METHODS:** A retrospective cohort study was conducted using the National Health Insurance Research Database between January 1997 and December 2008. The inclusion criteria were adult women who were newly diagnosed with breast cancer and without past history of hyperlipidemia or other cancer diseases between 1998 and 2008. The study endpoint was defined as emerging

of the first prescription of LLDs within the exposure period. Adjusted hazard ratio (HR) for the first LLDs prescription was analyzed using multivariable Cox proportional hazards regression model. **RESULTS:** There were 378, 1148 and 756 breast cancer patients treated with AIs, tamoxifen and didn't receive hormonal therapy, respectively. Compared to the non-hormonal therapy cohort, the rate of prescribing LLDs was lower in patients who treated with tamoxifen after adjusted age and comorbidity (HR=0.68, [95% CI=0.46-0.99]), and non-significantly increased in patients who treated with AIs (HR=1.12 [95% CI=0.65-1.91]). In addition, the prescribing LLDs rate between AIs treatment and treatment with tamoxifen was non-significantly increased (HR=1.41 [95% CI=0.83-2.83]) in the head to head comparison. **CONCLUSIONS:** Results from this study indicated that AIs does not significantly increase the risk of prescribing LLDs compare to the patients without hormonal therapy. In contrast, the tamoxifen therapy was significantly reduced the prescription rate of LLDs, thus tamoxifen might had potential benefit on lipid metabolism.

PCN3

IMPROVEMENT OF THE 3RD GENERATION COLORECTAL CANCER GENE CHIP

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OBJECTIVES: Colorectal Cancer (CRC) has now become the second leading cause of death in Taiwan, and is one of the cancers with highest incidence in women. Our goal is to integrate comprehensive information to determine the relation between omics and clinical pathology by a systematic biomedical approach and further improve our third generation gene chips for higher sensitivity and specificity toward colorectal cancer. **METHODS:** One hundred and five patients colorectal cancer patients who had undergone curative surgical resection of colorectal cancer were studied. The copy number for each SNP probe set taken from a tumor sample was calculated by comparing the probe intensity to the reference probe intensity from non-neoplastic tissue, and creating a list of the genome-wide copy number data. **RESULTS:** Among 105 patients with a median follow-up period of 5.6 years (range, 4.1-10.8 years), 23 developed early disease recurrence, whereas 82 did not. Most of them were male and less than 60 years ($p=0.044$). Stage III, deeper invasive tumor (T3+ T4) and positive lymph node metastasis could be found seriously by 70.5%, 92.4%, and 68.6%, respectively. CEA, EV12B, ATP2A2, S100B, KLK7, TM4SF3, and OLFM4 had copy number gains and high expression levels ($p < 0.05$) in no recurrence vs. recurrence. **CONCLUSIONS:** Patients less than 60 years were significantly risky to get early relapse in colorectal cancer. In comparison to traditional colorectal cancer gene chip, we would weight higher on EV12B (RR 4.622, 95% CI 1.741-12.270, $p=0.001$), ATP2A2 (RR 4.688, 95% CI 1.443-15.232, $p=0.006$), and S100B (RR 11.521, 95% CI 2.688-49.377, $p=0.0001$).

PCN4

ROLE OF 5-ALPHA-REDUCTASE INHIBITORS, STATINS, ASPIRIN, NSAIDS ON THE DEVELOPMENT OF PROSTATE CANCER IN BENIGN PROSTATIC HYPERPLASIA PATIENTS-A POPULATION BASED STUDY

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OBJECTIVES: The 5-alpha-reductase inhibitors (5-ARIs), statins, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) were previously reported to have protection effect for prostate cancer. The aim of this study was to simultaneously investigate these drug effects on prostate cancer risk among benign prostatic hyperplasia (BPH) patients. **METHODS:** Newly diagnosed BPH patients (ICD-9-CM code: 185 and A-code: A124) with at least one prescription of BPH medications (5-ARIs, alpha-blockers) were identified from Taiwan Longitudinal Health Insurance Database 2000 in 1998-2008. Drug usages of 5-ARIs, statins, aspirin, traditional NSAIDs (tNSAIDs), and cyclooxygenase-2 (COX-2) selective inhibitors were computed in terms of define daily dose (DDD), and were further categorized into high and lose dose groups by medians. The Cox regression was used to estimate hazard ratios (HRs) for the occurrence of prostate cancer. Additional covariates in the model included age, time-dependent covariates of drug usages and Charlson comorbidity score. **RESULTS:** There were 758 prostate cancers indicated from the registry dataset for catastrophic illness patients from 41,955 BPH patients. The analysis of all studied drugs showed significant protection HRs from univariate analyses. After adjusting for covariates, the multivariable analysis showed significant protection effects on high dose of 5-ARIs (HR=0.47, 95%CI= 0.26-0.99), on high dose of statins (HR=0.56, 95%CI= 0.38-0.83), on both low and high dose of tNSAIDs (HR=0.42, 95%CI= 0.36-0.50; HR=0.25, 95%CI= 0.20-0.31), and on both low and high dose of aspirin (HR=0.73, 95%CI= 0.60-0.88; HR=0.34, 95%CI= 0.26-0.45). The COX-2 selective inhibitors became not significant. **CONCLUSIONS:** The 5-ARIs, statins, tNSAIDs, aspirin and COX-2 selective inhibitors have been separately investigated their protection effects on the development of prostate cancer. Our results indicated that the protection effects of 5-ARIs, statins, tNSAIDs and aspirin were independently significant. In addition, the protection effect from COX-2 selective inhibitors was appeared to be confounded by other medication.

PCN5

IMPACT OF ERYTHROPOIESIS STIMULATING AGENTS ON SURVIVAL AMONG PATIENTS WITH COLORECTAL CANCER RECEIVING CHEMOTHERAPY

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OBJECTIVES: To evaluate the effect of Erythropoiesis stimulating agents (ESAs) use on survival among colorectal cancer patients undergoing chemotherapy. **METHODS:** This study was a nonconcurrent prospective cohort study using the